REMARKS

Claims 22-30 are pending. Claims 23, 24, and 26-28 are rejected under 35 U.S.C. § 112, second paragraph, claims 22-30 are rejected under 35 U.S.C. § 112, first paragraph, and under the judicially created doctrine of obviousness-type double patenting. Applicants address each of these rejections as follows.

Claim Amendments

Claim 1 has been amended to recite that the extracellular portion of the receptor includes a CD4 portion that specifically recognizes and binds HIV or an HIV-infected cell, where the CD4 portion is projected away from the membrane of a cell bearing the receptor by at least 48 angstroms, and where the extracellular portion does not mediate HIV infection. Support for this amendment is found, for instance, in Example X of the specification as filed. In view of the amendment to claim 22, claim 27 has been canceled and the dependency of claim 28 has been amended. For the record, Applicants note that the present amendments were made solely to expedite prosecution, and Applicants reserve the right to pursue all canceled subject matter in this or a related, future application.

In addition, claim 26 has been amended to recite SEQ ID NO: 33. Support for this amendment is found, for example, in Figure 25. No new matter has been added by the present amendments.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 23, 24, and 26-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claim 27 has been canceled and the rejection of this claim, therefore, is moot. The Office notes that SEQ ID NO:32 recited in claim 26 refers to a nucleic acid sequence and not an amino acid sequence. Claim 26 has been amended to recite SEQ ID NO:33, the sequence of which is the amino acid sequence encoded by SEQ ID NO:32. In addition, claim 1, as amended, provides antecedent basis for the term "CD4 portion" recited in claims 23, 24, and 28. The indefiniteness rejection of claims 23, 24, and 28 should be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 22-30 are rejected under 35 U.S.C. § 112, first paragraph, on the assertion that the specification fails to comply with the written description requirement and that the specification fails to enable the full scope of the claims. As noted above, claim 27 has been canceled and the rejection of this claim is moot. With regard to the remaining claims, Applicants address the written description and enablement bases for rejection below.

Written Description

The Office asserts (page 3):

> [T]he specification does not implicitly or inherently teach of CD4 domains that do not mediate HIV infection. The specification does not teach which CD4 domain(s) ... are capable of performing the function that is required of the CD4 component of the instantly claimed invention.

This rejection should be withdrawn.

Claim 1, as amended, requires that the extracellular portion of the receptor includes a CD4 portion that specifically recognizes and binds HIV or an HIV-infected cell, where the CD4 portion is projected away from the membrane of a cell bearing the receptor by at least 48 angstroms, and where the extracellular portion does not mediate HIV infection. The specification as filed meets the written description requirement for the extracellular portions and CD4 portions recited in the present claims.

As an initial matter, Applicants note that the claims, as amended, clarify that it is the extracellular portion that does not mediate HIV infection and not the CD4 component of the extracellular portion. Extracellular portions having the function required by the present claims are described in the application as filed. For instance, in Example X, Applicants' specification describes multiple chimeric receptors with extracellular portions that do not mediate HIV infection (see, e.g., Table 1). The specification teaches:

> From the data presented in Table 1, we concluded that the extracellular domains of CD4 should optimally be projected away from the cell membrane by at least 48 angstroms ... in order to resist HIV-1 infection. (page 16, lines 20-24)

As noted above, the claims, as amended, require the CD4 portion to be projected at least

48 angstroms away from the host cell membrane. There can be no question that the specification describes extracellular portions containing a CD4 portion that is projected at least 48 angstroms away from the host cell membrane, where the extracellular portion resists HIV infection.

Moreover, Applicants' specification describes CD4 portions that specifically recognize and bind HIV or HIV infected cells. For example, the specification teaches:

> Fig. 5A-C shows that HeLa cells expressing gp120/41 were specifically lysed by cytotoxic T lymphocytes (CTL) expressing CD4 chimeras. Uninfected HeLa cells were not targeted by CTL armed with CD4:ζ chimeras, and HeLa cells expressing gp120/41 were not recognized by uninfected CTL. (page 37, lines 17-22)
>
> * * *
>
> [A] chimera composed of the extracellular domain of CD4 fused to the ζ chain in a human CTL clone, WH3, specifically kills target cells displaying the surface envelope glycoprotein of HIV-1, gp120. (page 51, lines 18-22)
>
> * * *
>
> Binding studies with soluble ^{125}I-labelled gp120 established that both CD4(D1-D4):Ig:CD7 and CD4(D1, D2):Ig:CD7 had uncompromised affinity for gp120. (page 53, lines 17-19)

As evidenced by the cited sections of the specification, the CD4 portions recited in the present claims are described in the application as filed. Clearly, the specification not only describes extracellular portions that do not mediate HIV infection and that contain a CD4 portion that is projected at least 48 angstroms away from the host cell membrane, but also exemplary CD4 portions that specifically recognize and bind HIV or HIV infected cells.

Applicants' specification describes what is claimed. The written description basis for rejection should be withdrawn.

Enablement

Claims 22-30 are rejected based on the assertion that the specification does not enable a person skilled in the art to make the invention commensurate in scope with the claims. In particular, the Office asserts (pages 6):

> [T]he specification does not teach which CD4 domains specifically recognize and bind HIV or an HIV infected cell but do not mediate HIV infection.

As noted above in the section addressing the written description rejection, the amendments to claim 1 clarify that it is the extracellular portion of the claimed chimeric receptors that does not mediate HIV infection. The extracellular portion contains a CD4 portion that specifically recognizes and binds HIV or an HIV infected cell. The specification provides numerous examples of how one skilled in the art can make and use a chimeric receptor having such a CD4 portion. (See, e.g., Example II, entitled "Construction of CD4 Receptor Chimeras" and Example VI entitled "CD4:ζ, η, and γ Chimeras Mediate Cytolysis of Targets Expressing HIV gp120/41.")

In addition, the specification, for instance, in Example X, describes how to position a CD4 extracellular portion away from the host cell membrane using various portions of membrane-bound receptors, as well as synthetic alpha helices. Further, for example, in Table 1 at page 58, the specification provides multiple working examples of

extracellular portions that contain a CD4 portion, where the extracellular portion does not mediate HIV infection. As such, Applicants submit that the specification describes the chimeric receptors encompassed by the present claims and enables one skilled in the art to make and use such chimeric receptors without undue experimentation. This basis for the enablement rejection should be withdrawn.

The Office also asserts (page 7):

> [T]he specification discloses that the distance in which the CD4 domains of the extracellular portion of the chimera receptor project itself [sic] from the cell membrane is critical to infectivity of HIV ... However, such criticality is not recited in the claims, with the exception of claims 26-28 [sic; claims 27-28].

Applicants note that claim 1, as amended, includes the limitation of canceled claim 27 and now requires that the CD4 portion be projected away from the membrane of a cell bearing the receptor by at least 48 angstroms. The present claims are free of this basis for rejection.

Obviousness-Type Double-Patenting

Claims 22, 25, and 29-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent Number 5,843,728 ("the '728 patent"), claim 22 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent Number 6,392,013 ("the '013 patent"), and claims 22-30 are rejected under

the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-14 of U.S. Patent Number 6,753,162 ("the '162 patent"). As previously noted, claim 27 has been canceled and the rejection of this claim is moot. Applicants address the remaining rejections as follows.

The '728 Patent and the '013 Patent

The claims of the '728 patent and of the '013 patent fail to describe or suggest an extracellular portion of a chimeric receptor that includes a CD4 portion that specifically recognizes and binds HIV or an HIV-infected cell, where the CD4 portion is projected away from the membrane of a cell bearing the receptor by at least 48 angstroms, and where the extracellular portion does not mediate HIV infection. Given that the claims of neither the '728 patent nor the '013 patent teach or suggest all of the features of the presently claimed invention, the obviousness-type double patenting rejection over these patents should be withdrawn.

The '162 Patent

Applicants hereby acknowledge the obviousness-type double patenting rejection over the '162 patent and agree to address this basis for rejection upon the indication of otherwise allowable subject matter in the present application.

CONCLUSION

Applicants submit that the application is now in condition for allowance, and this action is hereby respectfully requested.

Enclosed are a Petition to extend the period for replying to the Office Action for three (3) months, to and including September 22, 2005, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 22 September 2005

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